## 1.0 OBJECTIVES

### 1.1 Primary Objective:

To determine the percentage of patients with high risk neuroblastoma in first or subsequent partial response or better, or with microscopic residual bone marrow disease, who demonstrate an immunological anti-tumor response at any time during, and for up to 12 months from initiation of, treatment with subcutaneous injections of autologous neuroblastoma cells, genetically modified by adenoviral vectors to secrete interleukin-2 (IL-2) (autologous neuroblastoma vaccine)

### 1.2 Secondary Objectives:

1.21 To determine the toxicity of the autologous neuroblastoma vaccine given according to this schedule

1.22 To obtain preliminary data on progression-free survival from high-risk neuroblastoma following vaccine administration

## 2.0 BACKGROUND AND RATIONALE

Neuroblastoma is the most common extracranial solid tumor in children. It affects nearly 500 new children each year. Approximately 60% of these children will have high-risk disease, that is, disease which by virtue of its anatomic distribution (widely disseminated, Stage 4) or inherent biology (Shimada unfavorable histology or N-myc amplification) carries with it greater than 60% chance of relapse or progression within 3 years of diagnosis (1-6). Once relapse or progression occurs, long-term survival is extremely rare. Over the past two decades, attempts to increase the chance of survival for children newly diagnosed with high-risk disease have focused on dose-intensification of chemotherapy, primarily achieved through the use of marrow or stem cell rescue, and on the introduction of new agents. Although rates of complete and partial remission of greater than 70% have been achieved and length of survival has increased with these approaches, there has been no significant improvement in the ultimate rate of survival. In the recently

conducted Children's Cancer Group (CCG) clinical trial of bone marrow transplantation versus continued chemotherapy for high-risk neuroblastoma, three year event-free survival was significantly better from patients treated with transplant but still only 34% (7). In a non-randomized study of bone marrow transplant versus none conducted by the Pediatric Oncology Group (POG), four-year survival was 29% for patients treated with transplant (8). Clearly, new treatment methods for increasing long term survival rates for high-risk neuroblastoma patients are needed. New approaches include treatment beyond transplantation and use of immune modulation (9, 10).